UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/732,998	12/07/2000	Hilary A. Coller	2825.2006-001	3011

21005 7590 07/02/2003

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	16

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/732,998	COLLER ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 21-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This Action is in response to the communication filed on 4/8/03, as Paper No. 15. Claims 1-35 are presently pending in the application and are addressed herein.

2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Election/Restrictions

3. Claims 1-12 and 21-35 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention for the reasons of record, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

4. Claims 13-20 are examined herein.

Claim Rejections - 35 USC § 103

5. Applicant's arguments, see page 2 through page 4 of the response filed 4/8/03, with respect to the rejection(s)of claim(s) under 35 USC 103 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made for the reasons set forth below.

New Grounds of Rejection

Claim Rejections - 35 USC § 112, second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 13 recites the limitation "the gene" in line 1. There is insufficient antecedent basis for this limitation in the claim; therefore, it is unclear what the phrase "the gene" refers to. Claims 14-20 are dependent claims and, therefore, are rejected for the same reason.

9. It is noted that amending claim 13 such that line 11 recites, "such that if the effect of MYC on gene expression is enhanced or..." would obviate this rejection.

Claim Rejections - 35 USC § 112, first paragraph

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 13-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a method for identifying an agent that regulates MYC-dependent transcriptional regulation of gene expression utilizing a cell that expresses a chimeric receptor, a ligand that activates the chimeric receptor, and a test compound that may modulate MYC's transcriptional ability. The claims are very broad and encompass a chimeric receptor that is a transmembrane receptor, as well as a non-transmembrane receptor. Furthermore, as presently written the ligand binding domain of the chimeric receptor could be a ligand binding domain for any type of ligand, including hormone as well as non-hormone ligands.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164)

The instant claims encompass transmembrane as well as non-transmembrane chimeric receptors comprising MYC and a ligand binding domain wherein the ligand binding domain can bind hormone as well as non-hormone ligands. However, the specification only explicitly discloses a non-transmembrane chimeric receptor that comprises MYC and a ligand binding domain that binds to estrogen (or estrogen analogs). The specification does not explicitly disclose any other types of chimeric receptors, such as: (1) a transmembrane receptors comprising MYC and a ligand binding domain for a non-hormone ligand, and (2) a non-transmembrane receptor comprising MYC and a non-hormone ligand binding domain. Therefore

the claims clearly encompass molecules for which there is insufficient written description provided in the specification. The specification has not identified the non-transmembrane receptors comprising MYC and a non-hormone ligand binding domain or the non-hormone ligands which could be "contacted" to the cells expressing the chimeric receptor and result in the activation of the intracellular receptor. Furthermore, there is no description of the transmembrane receptors comprising MYC and a ligand binding which can be activated to induce MYC regulated gene transcription when the appropriate ligand is used. The specification does not indicate any attributes or domains which would be common to all ligands encompassed by the claims, nor does the specification disclose the attributes common to all members of the chimeric receptors. Furthermore, the prior art does not teach that there are any transmembrane receptors comprising MYC and a ligand binding domain which, when activated by an appropriate ligand, can result in the induction of MYC regulated gene transcription. Nor does the prior art teach any non-hormone ligands which could be "contacted" to the cells expressing the intracellular non-transmembrane chimeric receptors and result in the diffusion of the ligand into the cell where it results in the activation of the chimeric receptor and induction of MYC regulated gene transcription.

12. Claims 13-20 are rejected under 35 U.S.C. 112, first paragraph (in view of the written description rejection), because the specification, while being enabling for:

> A method for identifying an agent that regulates MYC-dependent transcriptional regulation of gene expression comprising the steps of:

(a) obtaining an indicator cell that expresses a chimeric receptor that is a non-transmembrane chimeric receptor comprising MYC and a hormone binding domain;
(b) contacting said indicator cell with an appropriate hormone in the presence and absence of an agent to be evaluated for its ability to regulate MYC's transcriptional regulation activity;

and steps (c) and (d) as set forth in pending claim 13;

such that if the effect of MYC on gene expression is enhanced or inhibited in the presence and not the absence of the agent, then the agent regulates MYC-dependent transcriptional regulation of gene expression;

does not reasonably provide enablement for the full scope encompassed by the claims (e.g., a transmembrane chimeric receptor). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The instant claims are drawn to a method for identifying an agent that regulates MYC-dependent transcriptional regulation of gene expression utilizing a cell that expresses a chimeric

receptor, a ligand that activates the chimeric receptor, and a test compound that may modulate MYC's transcriptional ability.

The breadth of the claims

The present claims are broad enough to encompass a chimeric receptor that is a transmembrane receptor comprising an extracellular ligand binding domain and an intracellular domain comprising MYC, as well as a non-transmembrane receptor comprising MYC and a ligand binding domain. Furthermore, the ligand binding domain could be any type of ligand binding domain including a hormone binding domain as well as non-hormone binding domains.

The unpredictability of the art and the state of the prior art

As mentioned above, the claims encompass utilizing a cell the expresses a chimeric receptor wherein the chimeric receptor can be a transmembrane chimeric receptor, or a non-transmembrane chimeric receptor. Furthermore, the chimeric receptor can comprise MYC and a ligand binding domain wherein the ligand binding domain can be binding domain for any ligand, such as a hormone binding domain and non-hormone binding domains.

Regarding the chimeric receptor, the only known chimeric receptors comprising MYC and a ligand binding domain are non-transmembrane chimeric receptors comprising MYC and a hormone binding domain, such as the MYC-estrogen receptor chimera described by Eilers. Eilers (as mentioned in a previous Office Action) teaches a Rat1a cell expressing a MYC-estrogen receptor chimera that is activated when the cell is treated with estrogen. The prior art does not indicate that there were any transmembrane chimeric receptors comprising MYC and a ligand binding domain that is transcriptionally active when activated by the appropriate ligand.

Regarding the non-transmembrane receptor, it was well known that MYC is a transcription factor that activates the transcription of MYC-responsive genes. In order for MYC to activate transcription MYC must be present in the nucleus of the cell. If the cell expresses a transmembrane chimeric receptor one of skill in the art would not expect the transmembrane receptor to be able to translocate to the nucleus where it would be required to be in order to activate transcription.

Regarding the non-transmembrane receptor, the claim is very broad and encompasses a non-transmembrane receptor comprising MYC and a ligand binding domain wherein the ligand binding domain can be a hormone or non-hormone binding domain. If the chimeric receptor comprises a non-hormone ligand binding domain and the cell is "contacted" by the ligand, it is unclear how the non-hormone ligand would be able to enter the cell as hormones were the only known ligands which could readily pass through the cell membrane. Therefore, if a non-transmembrane receptor was treated with a non-hormone ligand, one of ordinary skill in the art would not expect the ligand to be able to enter the cell and activate the receptor.

Working Examples and Guidance in the Specification

The only working example provided in the specification is a cell that expresses a chimeric receptor comprising the ligand binding domain of the estrogen receptor and MYC (MYC-ER). This chimeric receptor (MYC-ER) is a non-transmembrane receptor that is activated by estrogen or OHT (an estrogen analog). When the cells that express MYC-ER are treated with estrogen or OHT, the estrogen or OHT is able to enter the cell, bind to the ER-binding domain of the chimeric receptor and activate MYC's transcriptional activity resulting in the transcription of MYC regulated genes.

There are no working examples provided wherein the receptor is a transmembrane receptor, nor are there any examples wherein the appropriate ligand to be used isn't a hormone (or analog thereof).

Quantity of Experimentation

Considering the breadth of the claims, additional experimentation would be required in order to determine how to activate a non-transmembrane chimeric receptor with a non-hormone ligand such that "contacting" the cell expressing the non-transmembrane receptor would be activated by the non-hormone ligand. Furthermore, additional experimentation would be required to determine how a transmembrane receptor comprising MYC and a ligand binding domain could activate MYC regulated gene transcription. Considering the transmembrane receptor would be attached to the cell membrane, one of skill in the art would not expect it to be able to translocate to the nucleus and activate transcription.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the breadth of the claims, the limited of working examples and guidance in the specification, the high degree of skill required, and the problems associated with (1) using a transmembrane receptor to activate MYC regulated gene transcription and (2) using a non-hormone ligand to activate a non-transmembrane receptor which would be obvious to one of skill in the art, it is concluded that the amount of experimentation required to perform the broadly claimed invention is undue.

Conclusion

No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell
June 30, 2003

DAVE T. NGUYEN
PRIMARY EXAMINER